



UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

10D

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/699,518	10/31/2003	David M. Armistead	A-748F	4199

7590 07/06/2004

U.S. Patent Operations/JWB
Dept. 4300, M/S 27-4-A
AMGEN, INC.
One Amgen Center Drive
Thousand Oaks, CA 91320-1799

EXAMINER
BALASUBRAMANIAN, VENKATARAMAN

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 07/06/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/699,518	ARMISTEAD ET AL.	
	Examiner Venkataraman Balasubramanian	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) Responsive to communication(s) filed on _____.
- 2a) This action is **FINAL**. 2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) Claim(s) 1-31 is/are pending in the application.
 - 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) Claim(s) _____ is/are allowed.
- 6) Claim(s) 1-31 is/are rejected.
- 7) Claim(s) _____ is/are objected to.
- 8) Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on _____ is/are: a) accepted or b) objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All b) Some * c) None of:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date: _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date <u>10/31/2003</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Claims 1-31 are pending.

Information Disclosure Statement

References cited in the Information Disclosure Statement, dated 10/31/2003, are made of record.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Following reasons apply. Any claim not specifically rejected is rejected as being dependent on a rejected claim and share the same scope.

1. Recitation of the phrase "comprising" in the definition of heterocyclic ring at various places of claim 1 and claim 13 renders these claims indefinite as the term is open-ended and can include more than what is being positively recited therein. See MPEP 2111.03 which states: The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., Genentech, Inc. v. Chiron Corp., 112 F.3d 495, 501, 42 USPQ2d 1608, 1613 (Fed. Cir. 1997) ("Comprising" is a term of art used in claim language which means that the named elements are essential, but other elements may be added and still form a construct within the scope of the claim.);

Molekulon Research Corp. v. CBS, Inc., 793 F.2d 1261, 229 USPQ 805 (Fed. Cir. 1986); In re Baxter, 656 F.2d 679, 686, 210 USPQ 795, 803 (CCPA 1981); Ex parte Davis, 80 USPQ 448, 450 (Bd. App. 1948) ("comprising" leaves "the claim open for the inclusion of unspecified ingredients even in major amounts")

2. The definition of haloalkyl in claim 1 is indefinite as it is not clear what is to be excluded as perhaloalkyl as recited therein. Specification has no definition of the term perhaloalkyl and hence it is not clear how many halo groups on the alkyl is to be treated as perhaloalkyl.
3. Compound claims 2-21, which depend on claim 1, do not indicate the variable groups are as defined in claim 1 and hence it is not clear what are these variable groups are.
4. The method of use claims 24-29 lack effective amount and therefore read on any or all amount.
5. The process claim 30 is indefinite for more than one reason. First of all, it is not clear what is definition of various variable groups. For example it is not clear what is R⁸. Secondly, the claim recites " each L is independently a leaving group as defined herein" but there is no such definition in the claim. Thirdly, the claim recites " a nucleophile of formula H-R¹" but all H-R¹ cannot be deemed as nucleophiles. See definition of R³ and R⁸.
6. The process claim 31 is indefinite for more than one reason. First of all the claim 31 lacks clarity as it recites "one or more of the formulae". Note reacting more than one triazine with a nucleophile would lead to mixture of products- a

composition- not a compound. Replacing "one or more" with "any one of" may obviate this rejection. Secondly, the scope of the claim is not clear. The claim recites nucleophilc agent or agents and as recited these agents could be any group. Thus the scope would be broader than claim 1 on which it is dependent. Again there are no definitions of variables.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 24-26 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating angiogenesis, does not reasonably provide enablement for treating all diseases embraced in the claim language of the instant invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The instant claims are drawn to 'a method for treating kinase-mediated disease or disease symptoms. Method claims 24-26 are not adequately enabled for the range of diseases recited therein. From the reading of specification, it appears that the applicants are asserting that the embraced compounds because of their mode action, which involves inhibition of kinase(s), would be useful for all sorts of diseases including autoimmune diseases, cancer, Alzheimer's disease, various arthritis, multiple sclerosis etc. However, the applicants have not provided any competent evidence that the instantly disclosed tests are highly predictive for all the uses disclosed and embraced by

the claim language for the intended mammal. That a single class of compounds can be used to treat all diseases embraced in the claims is an incredible finding for which applicants have not provided supporting evidence. Moreover many if not most of diseases such as rheumatoid arthritis, multiple sclerosis, Alzheimer's disease etc. are very difficult to treat and hardly possible to prevent as claimed herein. For multiple sclerosis alone there is no known drug, which can successfully reverse the course of the disease, despite the fact that there are many drugs, which can be used for "inflammatory condition". Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses. Next, applicant's attention is drawn to the Revised Interim Utility and Written Description Guidelines, at 64 FR 71427 and 71440 (December 21, 1999) wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed 'preventive' effect solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Traxler (provided in 09/685,053).

In evaluating the enablement question, several factors are to be considered. Note In re Wands, 8 USPQ2d 1400 and Ex parte Forman, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence

or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

- 1) The nature of the invention: Therapeutic use of the compounds in treating all diseases due to kinase inhibitory activity.
- 2) The state of the prior art: Although there are several kinase inhibitors known, they have not been able to treat all diseases embraced in the instant claims.
- 3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use for the 'treatment of all kinase mediated diseases' of the instant compounds. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).
- 4) The amount of direction or guidance present and 5) the presence or absence of working examples: There is no supporting evidence that all diseases embraced are treatable in view of their kinase activity.
- 6) The breadth of the claims: The instant claims embrace treatment of all or any diseases by inhibiting all or any kinase
- 7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of ligand-receptor interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards 'preventing' the variety of diseases of the instant claims, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 6, 8 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Giraldi et al. US 3,074,943.

Giraldi et al. teaches several substituted triazines for use as anti viral agents, which include compounds generically claimed in the instant claims. See formula I and note the definition of R', R'', and R''' on col.1. Note when R''' is hydrogen, the compounds taught by Giraldi include those claimed in the instant claims. See examples 1-5 for compounds made and the intermediates used for making on col.2-3.

Claims 1, 5-8, 22 and 30-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Cutler et al. US 3,097,205.

Cutler et al. teaches several disubstituted triazines, which include those, claimed in the instant claims for use as antibacterial agents. See formula I, III, IV, V, VI, VII and VII and note the definition of Y, Z and Z' on col. 1 through col. 3. Note the definition of Y, Z and Z' corresponds to instant R¹ and R². Also note the various choices of Z and Z' on col.2 and the process of making. See col. 3 –col.9 for examples of compounds made.

Claims 1, 6 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Cutler et al. US 3,209,003

Cutler et al. teaches several disubstituted triazines, which include those, claimed in the instant claims for use as antibacterial, antifungal and antiviral agents. See formula I and note the definition of X, R, Y¹ and Y² on col.1. Note the definition of X, R, Y¹ and Y² corresponds to compounds of instant R¹ and R². See examples 1-25 for various compounds made shown on col. 5 through 11.

Claims 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Fischer US 3,855,220.

Fischer teaches pyridinium-triazine and its intermediates which are also generically embraced in the instant claim. See compound of formula I and II on col. 1-2 and col. 4 and example 1.

Claims 1, 6 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Cutler et al. US 3,136,816

Cutler et al. teaches several disubstituted triazines, which include those, claimed in the instant claims for use as antibacterial, antifungal, antiviral agents and diuretic agents. See formula I and note the definition of X, R, and Y on col.1. Note the definition of X, R, Y and z corresponds to compounds of instant R¹ and R². See examples 1-7 for various compounds made shown on col. 3 through 8.

Claims 1, 6 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Thurston US 2,474,194.

Thurston teaches several substituted triazines, which include those, claimed in the instant claims. See formula I and note the definition of x, y and R, on col.1. Note the definition of x, y and R corresponds to compounds of instant R¹ and R². See examples 1-2 for compounds made shown on col. 2.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 6, 8-9 and 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Newton et al. US 5,062,882.

Newton et al. teaches several substituted triazines for use as herbicides. See formula I on col. 1 and note the definition of X, Y, Z, R1 and R². Note when one of R¹ and R² group is hydrogen, the compounds taught by Newton et al. include those claimed in the instant claims. See examples 1-72 on col.5-18 for compounds made.

Instant claims recite disubstituted triazine, i.e. the third substituent on the triazine carbon is hydrogen. Newton et al. does not teach hydrogen for either of R¹ and R² in compounds made.

However Newton et al. teaches the equivalency of exemplified substituents for R¹ and R² groups with that claimed. See cols.1, formula I, especially the definitions of R¹ and R² groups. As one trained in the art would expect the species of the genus behave similarly and possess the same use, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds variously substituted in triazine ring including species bearing hydrogen for R¹ or R² group as permitted by the reference and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Claims 1, 6, 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Riebel et al. US 6,284,710 (equivalent DE 196 41 693).

Riebel et al. teaches several substituted triazines for use as herbicides. See formula I on col. 1 and note the definition of X, Y, Z, R¹ and R². Note when Z is hydrogen, compounds taught by Riebel et al. include those claimed in the instant claims. See col. 6 through col. 58 for compounds made.

Instant claims recite disubstituted triazine, i.e. the third substituent on the triazine carbon is hydrogen. Riebel et al. does not teach hydrogen for Z in compounds made.

However Riebel et al. teaches the equivalency of exemplified substituents for Z groups with that claimed. See cols.1, formula I, especially the definition Z groups. As one trained in the art would expect the species of the genus behave similarly and

Art Unit: 1624

possess the same use, it would have been obvious to one having ordinary skill in the art at the time of the invention was made to make compounds variously substituted in triazine ring including species bearing hydrogen for Z group as permitted by the reference and expect resulting compounds to possess the uses taught by the art in view of the equivalency teaching outline above.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is Mukund Shah whose telephone number is (571) 272-0674. If Applicants are unable to reach Mukund Shah within 24-hour period, they may contact James O. Wilson, Acting-SPE of art unit 1624 at 571-272-0661.

The fax phone number for the organization where this application or proceeding is assigned (703) 872-9306. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

V. Balasubramanian
Venkataraman Balasubramanian

6/28/2004